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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/040,803	01/07/2002	Andrew Darrow	ORT-1562	4825

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EXAMINER	
MOORE, WILLIAM W	

ART UNIT	PAPER NUMBER
1652	6

DATE MAILED: 07/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,803	DARROW ET AL.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 6,9,12,13,15-20 and 23-27 is/are pending in the application.

4a) Of the above claim(s) 6,9,12,13,17-20 and 23-27 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 15 and 16 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 6,9,12,13,17-20 and 23-27 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Preliminary Amendment

Applicant's Preliminary Amendments A and B, Papers Nos. 2 and 6 filed January 7 and 30, 2002, have been entered, the former introducing at page 1 of the specification a statement of the relationship between the instant application and the parent application serial No. 09/386,629 and canceling claims 1-5, 7, 8, 10, 11, 14, 21 and 22, and the latter deleting the description of Figure 6 at page 3, lines 26-28, of the specification.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. §121:

I. Claims 6 and 9, drawn, if properly stated, to an expression vector comprising a genomic DNA molecule encoding a C-E protease and host cells comprising the nucleic acid sequence, classified in class 435, subclass 320.1.

II. Claims 12 and 13, drawn, if properly stated, to a monoclonal antibody, classified in class 530, subclass 387.1.

III. Claims 15 and 16, drawn, if properly stated, to a method of identifying a compound that modulates the activity of a C-E protease, classified in class 435, subclass 23.

IV. Claims 17, 18 and 20, drawn, if properly stated, to a compound that modulates protease C-E activity and to a method of use of the compound in treating a patient, classified, in the absence of a disclosure of the nature of such a compound, in class 514, subclass 1.

V. Claims 17, 19 and 20, drawn, if properly stated, to a compound that modulates the expression of the protease C-E and to a method of use of the compound in treating a patient, classified, in the absence of a disclosure of the nature of such a compound, in class 514, subclass 44.

VI. Claims 23-24 and 27, drawn, if properly stated, to a pharmaceutical composition comprising the C-E protease and use of a pharmaceutical composition in treating an imbalance of desquamation, classified in class 514, subclass 21.

VII. Claims 25 and 26, drawn, if properly stated, to a non-pharmaceutical composition comprising a C-E protease, classified in class 510, subclass 305.

Inventions Group I and Groups II-VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, functions, and effects.

Inventions Group II and Groups III-VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, functions, and effects.

Inventions of Groups III and Groups IV-VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together because the assay method of Group III requires no particular compound of either of Groups IV or V, nor may it utilize the compositions of Groups VI and VII, and because the assay method of Group III has modes of operation, functions, and effects that differ from those of the inventions of Groups IV-VII.

Inventions of Group IV and Groups V-VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, functions, and effects.

Inventions of Group V and Groups VI and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, functions, and effects.

Inventions of Group VI and Group VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, functions, and effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

During a telephone conversation with Ms. Myra McCormack on August 15, 2002, a provisional election was made with traverse to prosecute the invention of Group III, claims

15 and 16. Affirmation of this election must be made by applicant in replying to this Office action. Claims 6, 9, 12, 13, 17-20, and 23-27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC §112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15 and 16 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

A claimed method of identifying compounds modulating the activity of a C-E protease must be supported by a disclosure of (a) C-E protease(s) sufficient to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the genus of proteases to be used in the assay method. Claim 15, however, generically recites the term "protease C-E protein activity", thus does not exclude variant proteases from methods of claims 15 and 16, thus the claims are considered to include methods that utilize "functional derivatives" of the native C-E protease that are, according to pages 6-7 of the specification, "fragments" or "variants" of the amino acid sequence set forth in SEQ ID NO:7 or the amino acid sequence of the zymogen fusion with the C-E protease catalytic domain set forth in SEQ ID NO:8. There is no evidence in the specification that Applicant possessed a derivative, fragmentary, or variant protease having an amino acid sequence that diverges from that of SEQ ID NO:2 other than the zymogen fusion with the C-E protease catalytic domain set forth in SEQ ID NO:8 at the time the application was filed. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of 35 U.S.C. §112, first paragraph.

Fiers v. Revel v. Sugano, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification furnishes no relevant identifying characteristics of a protease that diverges in any way from the amino acid sequence of the C-E protease catalytic domain. In particular, the zymogen fusion protease having the amino acid sequence of SEQ ID NO:8 is an artificial product, a fusion polypeptide of heterologous domains, thus is not disclosed to be fragmentary in any respect and must possess the amino acid sequence of the native C-E catalytic domain.

In addressing the issue of whether a disclosure of a molecular structure of one polypeptide of one biological species could adequately describe the molecular structure of a functionally similar molecule of another biological species, the Court of Appeals for the Federal Circuit held that a claimed invention must be described with such "relevant identifying characteristic[s]" that the public could know that the inventor possessed the invention at the time an application for patent was filed, rather than by a mere "result that one might achieve if one had made that invention". *University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Indeed, the claims rejected herein are, like the claims invalidated by the appellate panel in *University of California v. Eli Lilly*, designed to embrace other, as yet unknown, human proteases. Nothing demonstrates that, at the time the specification was filed, Applicant was "able to envision" enough of the structure of an undisclosed generic protein to provide the public with identifying "characteristics [that] sufficiently distinguish it . . . from other materials". *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). While Applicant and others can replace, e.g., the native signal peptide of a human C-E protease, with a different signal peptide region just as Applicant introduced an alternative signal peptide, a polyhistidine tag, and an alternative propeptide region in preparing a baculovirus vector expression construct described in the specification, nothing in the specification shows that Applicant had determined, or had

even contemplated, which positions among the carboxyl-proximal 260 amino acids of the C-E protease might be altered, nor the nature of any amino acid substitution, nor any deletion of amino acids to generate a fragment. Thus the treatment of the claimed subject matter in the specification is considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could not predict the structure, or other properties, of generic C-E proteases to be used in methods of claims 15 and 16.

Claims 15 and 16 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a method of identifying compounds that modulate the activity of the human protease C-E having the amino acid sequence set forth in either SEQ ID NO:7 or SEQ ID NO:8, comprising combining a candidate compound with a human protease C-E comprising the catalytic domain of the amino acid sequence set forth in either SEQ ID NO:7 or SEQ ID NO:8 and a labeled substrate and measuring a change in the amount of the labeled substrate,

does not reasonably provide enablement for any and all method of identifying compounds that modulate the activity of "functional derivatives" of the human protease C-E. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 15 and 16 are rejected because claim 15, from which claim 16 depends, does not indicate that an C-E protease has the amino acid sequence set forth in either of SEQ IDs NOs:2 or 8 or that a contacting or combining step is practiced with the catalytic domain of the C-E protein, present in both of SEQ IDs NOs:7 and 8. Claim 15 recites the generic term "protease C-E protein", and in the absence of any definite structural limitation, must be construed as being drawn to "functional derivatives" of the human C-E protease embraced by canceled claims. The specification defines a "functional derivative" of a polypeptide, at page 6, as a molecule having a biological activity "substantially similar to" that of a disclosed polypeptide but Applicant enables only two proteases that clearly have proteolytic activity: the native human protease C-E having the amino acid sequence set forth in SEQ ID NO:7 and a very specific derivative of the native human protease C-E having the amino acid sequence set forth in SEQ ID NO:8. The amino acid sequence of SEQ ID NO:8 includes minor alterations of the amino-proximal region - or catalytic

domain - of the mature protease C-E due to incorporation of the corresponding region of the protease C-E cDNA in Applicants' expression vector to specify the PFEK-protease C-E-6XHIS product. The specification teaches no other alterations of the C-E catalytic domain.

The scope of the subject matter of a method for detecting modulatory compounds with an C-E protease that constitutes a "functional derivative" other than SEQ ID NO:7 or a functional derivative of SEQ ID NO:8 itself, is not enabled where it reaches arbitrary assignments of any or all of amino acid substitutions, additions or deletions in any number of amino acid positions in SEQ ID NO:2 or in SEQ ID NO:8, that would alter the primary structure of a human protease C-E in ways undisclosed in the specification. It is agreed that the specification discloses a specific modification of the amino acid sequence of SEQ ID NO:2, replacement of its signal peptide region with an heterologous signal peptide that a skilled artisan would readily be able to duplicate by selecting an alternate signal peptide. The specification, however, does not teach the carboxyl-terminal boundary of the signal peptide and fails to suggest such an alteration in any manner providing an adequate written description of this kind of alteration that may be recited in a claim.

Neither the prior art made of record herewith nor Applicant's specification identifies other amino acids in the proteolytic domains of, e.g., the closely related prior art prostasin and ß-tryptase proteases, that might be altered, nor teaches the nature of alterations that may be made, which would permit resulting variants to function as serine proteases. Mere sequence perturbation cannot enable design and preparation of nucleotide sequences encoding a myriad of divergent polypeptides and provide the public with undisclosed, generic, "protease C-E proteins". It is well settled that 35 U.S.C. §112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under

35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (recognizing and applying the "*Forman*" factors). Cf., *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) (citing eight factors relevant to analysis of enablement). The standard set by the CCPA, the predecessor of the present Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a reasonable correlation must exist between the scope of guidance provided by the specification and the scope asserted in the claimed subject matter. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone); **see also**, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (functional equivalency of divergent gene products not supported by disclosure only of a single B-cell growth factor allele). The standard set by the CCPA was approved by the Federal Circuit in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997).

An appellate panel recently considered whether definitional statements might enable a claim scope argued to extend beyond a disclosed, recombinantly-produced, gene product having its native amino acid sequence to embrace a specific variant gene product encoded by a specifically-altered DNA sequence. *Genentech, Inc. v. The Wellcome Found. Ltd.*, 29 F.3d 1555, 31 USPQ2d 1161 (Fed. Cir. 1994). The court held that only a narrow structural and functional definition was enabling precisely because the sweeping definitions of scope in the patent specification could not reasonably have been relied upon by the PTO in issuing the patent. *Genentech*, 29 F.3d 15 at 1564-65, 31 USPQ2d at 1168. Applying the "*Forman*" factors discussed in *Wands*, *supra*, to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the amino acid sequence of native human protease C-E other than preparation of SEQ ID NO:8,

b) the specification lacks working examples wherein the catalytic domain of the human protease C-E is further altered,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support random and arbitrary alterations, and,

d) unpredictability exists in the art where the catalytic domains of members of the class of proteases represented by the amino acid sequences of the proteases of Figure 2 enzyme have not yet been specifically modified.

Thus the scope of the claimed subject matter where claim 15 recites the generic term "protease C-E protein", cannot be considered to be supported by the present specification, even when taken in combination with the teachings available in the prior art. Limitation of the subject matters as indicated in the statement at page 6 above is required in order to overcome this rejection.

Claims 15 and 16 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is indefinite in reciting "protease C-E protein activity" because the addition of "protein" is ambiguous where it is open to an interpretation that some other function, not disclosed in the specification, is intended beyond that of a protease disclosed in the specification for the human protease C-E, i.e., it cleavage of peptide bonds. Claim 16 is also rejected because it fails to resolve the ambiguity of claim 15 from which it depends.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 15 is rejected under 35 U.S.C. §102(a) as being anticipated by Botstein et al., WO 99/35170, made of record with Applicant's Information Disclosure Statement.

Botstein et al. inherently disclose, in Figures 11, 12 & 34, SEQ IDs NOs:11 & 12, and at pages 18-20, 22-27, 31-44 and 48, the nucleotide sequence of a cDNA encoding a new, medically important, human serine protease, designated PRO343, having an amino acid sequence identical to the C-E protease herein. Because the native C-E/PRO343 protease catalytic domain is released by autoproteolysis from the native C-E/PRO343 precursor as well as from the fusion polypeptide of SEQ ID NO:8 upon expression, the activity of the released catalytic domain is indistinguishable in a claimed assay. Botstein et al. identify the PRO343 protease as a protease and their disclosure anticipates the subject matter of claim 15 herein because they disclose, pages 31-33, a method wherein an assayed compound may "interfere with", i.e., modulate, the activity of a PRO343 protease, and an assayed component "may be labeled by a detectable label", thus using the PRO343 protease to detect modulatory compounds.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(e), (f) or (g) prior art under 35 U.S.C. §103(a).

Claims 15 and 16 are rejected under 35 U.S.C. §103(a) as being anticipated by Chen et al., WO 99/14328, in view of Egelrud et al., U.S. Patent No. 5,834,290, both made of record with Applicant's Information Disclosure Statement.

Available as prior art under 35 U.S.C. §102(a), Chen et al. teach, see Figures 97 & 98, SEQ IDs NOs:262 & 263, and pages 29, 49-50, 59, 61-68, 79, 92-9, the nucleotide sequence of a cDNA encoding a new, medically important, human serine protease, designated PRO343, having an amino acid sequence identical to that of the C-E protease herein. Because the native C-E/PRO343 protease catalytic domain is released by autoproteolysis from the native C-E/PRO343 precursor as well as from the fusion polypeptide of SEQ ID NO:8 upon expression, the activity of the released catalytic domain is indistinguishable in a claimed assay. Chen et al. identify the PRO343 protease as a protease and they disclose, page 98, a method of using a PRO343 protease to detect compounds that may inhibit the interactions of the protease with other physiological molecules. Egelrud et al. teach, cols. 24-26, 30-32, and 48, the use of a newly-discovered, recombinantly-produced, and medically-important human serine protease, SCCE, in methods for the identification of compounds capable of modulating the catalytic activity of the serine protease, specifically, enhancing or inhibiting its catalytic activity, col. 24 at lines 16-26, wherein a method utilizes labeled, chromogenic, i.e., colormetric, substrates, particularly the S-2586 substrate, available from Boehringer and having their designation SEQ ID NO:15, and a similar chromogenic substrate having their designation SEQ ID NO:11. Egelrud et al. teach, col. 32, that they were better able to differentiate the activity of the new serine protease from known serine proteases, such as cathepsin G and chymotrypsin, by using the different chromogenic substrates.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to recombinantly express the new serine protease PRO343 taught by Chen et al. and to assay its catalytic activity utilizing several chromogenic substrates in order to identify compounds capable of modulating its activity, and in particular inhibiting its activity, according to the teachings of Egelrud et al. This is because Chen et al. consider the new

serine protease PRO343 to be of medical importance and because Egelrud et al. teach that the activity of a new, medically important, human serine protease can be differentiated from the activities of other known, medically important, human serine proteases by using several different chromogenic substrates.

Claim 15 and 16 are rejected under 35 U.S.C. §103(a) as being anticipated by Antalis et al., WO 98/36054, in view of Egelrud et al., U.S. Patent No. 5,834,290, both made of record with Applicant's Information Disclosure Statement.

Available as prior art under 35 U.S.C. §102(b), Antalis et al. teach, see Figure 20A, SEQ ID NO:28, pages 18 and 52-53 and claims 19-21, 26, and 27, the nucleotide sequence of a cDNA encoding a new, medically important, human serine protease, designated SP001LA, having a deduced amino acid sequence sharing 100% sequence identity with the amino acid sequence of the native C-E protease from position 47 to position 317, thus the catalytic domains of the prior art protease and the disclosed protease C-E are identical. Because the native C-E/SP001LA protease catalytic domain is released by autoproteolysis from the native C-E/SP001LA precursor as well as from the fusion polypeptide of SEQ ID NO:8 upon expression, the activity of the released catalytic domain is indistinguishable in a claimed assay. Antalis et al. identify the SP001LA protease as a protease and discuss, pages 25-26, the development of agonists, antagonists, and other modulatory compounds that can alter the activity of a disclosed protease. Egelrud et al. teach, cols. 24-26, 30-32, and 48, the use of a newly-discovered, recombinantly-produced, and medically-important human serine protease, SCCE, in methods for the identification of compounds capable of modulating the catalytic activity of the serine protease, specifically, enhancing or inhibiting its catalytic activity, col. 24 at lines 16-26, wherein a method utilizes labeled, chromogenic, i.e., colormetric, substrates, particularly the S-2586 substrate, available from Boehringer and having their designation SEQ ID NO:15, and a similar chromogenic substrate having their designation SEQ ID

NO:11. Egelrud et al. teach, col. 32, that they were better able to differentiate the activity of the new serine protease from known serine proteases, such as cathepsin G and chymotrypsin, by using the different chromogenic substrates.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to recombinantly express the new serine protease SP001LA taught by Antalis et al. and to assay its catalytic activity utilizing several chromogenic substrates in order to identify compounds capable of modulating its activity, and in particular inhibiting its activity, according to the teachings of Egelrud et al. This is because Antalis et al. consider the new serine protease PRO343 to be of medical importance and because Egelrud et al. teach that the activity of a new, medically important, human serine protease can be differentiated from the activities of other known, medically important, human serine proteases by using several different chromogenic substrates.

Claim 16 is rejected under 35 U.S.C. §103(a) as being unpatentable over Botstein et al. as applied to claim 15 above, and further in view of Egelrud et al., U.S. Patent No. 5,834,290, made of record with Applicant's Information Disclosure Statement.

The teachings of Botstein et al., discussed above, are taken as before. Egelrud et al. teach, cols. 24-26, 30-32, and 48, the use of a newly-discovered, recombinantly-produced, and medically-important human serine protease, SCCE, in methods for the identification of compounds capable of modulating the catalytic activity of the serine protease, specifically, enhancing or inhibiting its catalytic activity, col. 24 at lines 16-26, wherein a method utilizes labeled, chromogenic, i.e., colormetric, substrates, particularly the S-2586 substrate, available from Boehringer and having their designation SEQ ID NO:15, and a similar chromogenic substrate having their designation SEQ ID NO:11. Egelrud et al. teach, col. 32, that they were better able to differentiate the activity of the new serine protease from known serine proteases, such as cathepsin G and chymotrypsin, by using the different chromogenic substrates.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to recombinantly express the new serine protease PRO343 taught by Botstein et al. and to assay its catalytic activity utilizing several chromogenic substrates in order to identify compounds capable of modulating its activity, and in particular inhibiting its activity, according to the teachings of Egelrud et al. This is because Botstein n et al. consider the new serine protease PRO343 to be of medical importance and because Egelrud et al. teach that the activity of a new, medically important, human serine protease can be differentiated from the activities of other known, medically important, human serine proteases by using several different chromogenic substrates.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached between 9:00AM-5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached at 703.308.3804. Further fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
July 1, 2003